Remarks

This Amendment is responsive to the Official Action mailed March 11, 2003 (Paper No. 9). Entry of this Amendment and reconsideration of the subject application in view thereof are respectfully requested.

Claims

Claims 25, 27, 29, 31, 32, 43-44 and 46 were pending. Claims 26, 28, 30, 33, 34, 35, 36-42, 45 and 47-49 were withdrawn as being drawn to the non-elected invention. Claims 25, 27, 29, 31, 32, 43-44 and 46 stand rejected.

It is believed that entry of this Amendment is timely filed. Notwithstanding, Applicants hereby authorize the Commissioner to charge any additional claim fees and/or extension of time fees required by entry of this Amendment to Deposit Account No. 50-0258.

Claims 26, 28, 30, 33, 34, 35, 36-42, 45 and 47-49 have been cancelled as being drawn to the non-elected invention. Claims 25, 43 and 44 have been amended to more clearly recite the present invention. Support for this amendment is apparent. Thus, no new matter is added.

Specification

The specification was objected to for not containing an abstract and for not beginning the claim section with the phrase, "I claim." Applicants enclose herewith as Appendix B a copy of the abstract as published in the PCT priority application. Further, Applicants have amended the claim section to begin with the phrase, "I claim" as recited in Appendix C. Withdrawal of objections is respectfully requested.

Claim Rejections under 35 U.S.C. §112, first paragraph

Claims 25, 27, 29, 31, 32, 43-44 and 46 were rejected under 35 U.S.C. 112, first paragraph for written description. In particular, the Examiner alleged

> The specification describes the polypeptide SEQ ID NO: 2, (see page 1-9) from Neisseria meningitidis comprising 722 amino acids. The actual biological function of the polypeptide, SEQ ID NO: 2 is not set forth in the specification. Applicants broadly describe the fragments of SEQ.ID.NO: 2 obtained by embracing

any substitution, insertion or deletion of amino acid throughout the entire stretch of polypeptide by use of language in which a fragment sequence of 15 amino acids or 20 amino acids that matches an aligned contiguous segment of SEQ.ID.NO: 2. None of these fragments meets the written description provision of 35 U.S.C. 112, first paragraph. Vas-Cath Inc. v. Mahurkar, 19 USPQ2d 1111, makes clear that "applicant must convey with reasonable clarity to those skilled in the art that, as of the filing date sought, he or she was in possession of the invention. The invention is, for purposes of the 'written description' inquiry, whatever is now claimed." (See page 1117.) The specification does not "clearly allow persons of ordinary skill in the art to recognize that (he or she] invented what is claimed." (See Vas-Cath at page 1116.).

The specification fails to teach a single fragment of a polypeptide sequence of SEQ ID NO: 2 and it is noted that the claimed polypeptides do not exist as an invention independent of their function in a putative outer membrane polypeptide. The actual structure or other relevant identifying characteristics of each fragment having the claimed properties of the polypeptide can only be determined empirically by actually making every amino acid which can result in fragments with 15 or 20 amino acids and testing each to determine whether it is a polypeptide having the particularly disclosed properties of an BASBO53 polypeptide.

There must be some nexus between the structure of the polypeptide fragments and the function of that fragment. The specification fails to teach the structure or relevant identifying characteristics of a representative number of species of a representative number of polypeptides, sufficient to allow one skilled in the art to determine that the inventor had possession of the invention as claimed. With the exception of an isolated polypeptide comprising SEQ ID NO: 2, fragments comprising 15 or 20 amino acids the skilled artisan cannot envision the contemplated sequences by the detailed chemical structure of the claimed fragments regardless of the complexity or simplicity of the art. Adequate written description requires more than a mere statement that it is part of the invention and reference to a potential method for making it. See Fiers v. Revel, 25 U5PQ2d 1601, 1606 (CAFC 1993) and Amgen Inc V Chuaai Pharmaceutical Co Ltd., 18 U5PQ2d 1016. One cannot describe what one has not conceived. See Fiddes v. Baird, 30 U5PQ2d 1481, 1483. In Fiddes v. Baird, claims directed to mammalian FGF's were found unpatentable due to lack of written description for the broad class.

Applicants traverse this rejection. Sufficient description of the present invention is provided in the specification. Disclosure of SEQ ID NO:2 and the working examples found on pages 52-54 demonstrate that Applicant was in possession of the invention as claimed. As explained below in response to the Examiner's rejection of enablement, one of ordinary skill in the art could make and use claims directed to an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids that matches an aligned contiguous segment of SEQ ID NO:2 based on the disclosure in the present application. Accordingly, Applicants respectfully request withdrawal of this rejection.

Claims 25, 27, 29, 31, 32, 43-44 and 46 were rejected under 35 U.S.C. §112, first paragraph for enablement. In particular, the Examiner alleged:

> Instant claims are evaluated for enablement using Wands analysis. Many of the factors regarding undue experimentation have been summarized in In re Wands, 858 F.2d 731,8 USPQ2d 1400 (Fed.Circ.1988) as follows:
>
> (1) the nature of the invention, (2) the state of the prior art, (3) the predictability or lack thereof in the art, (4) the amount of direction or guidance present, (5) the presence or absence of working examples, (6) the quantity of experimentation necessary, (7) the relative skill of those in the art, and (8) the breadth of the claims.
>
> The specification fails to indicate the biological activity of SEQ ID NO: 2, fails to teach that SEQ ID NO: 2, a polypeptide that is detected by immune or convalescent sera and further lacks any description of polypeptide SEQ ID NO: 2 which acts as a vaccine comprising a fragment sequence of at least 15 or 20 amino acids that matches contiguous segment of SEQ.ID.NO: 2. The specification is not enabled for any immunogenic polypeptide comprising a fragment sequence of at least 15 or 20 amino acids that matches contiguous segment of SEQ.ID.NO: 2, because 1) the specification fails to teach that the alleged polypeptide SEQ ID NO: 2 is able to function as a vaccine 2) the specification fails to teach how to make and use fragments thereof that have an unknown and uncharacterized function; 3) the specification fails to teach what are the critical residues that can be modified and still achieve a fragment with any functional activity or any fragments with vaccine characteristics for Neisseria meningitidis, - 4) the art teaches that polypeptides with replacement of single amino acid

residues may lead to both structural and functional changes in biological activity and immunological recognition, one skilled in the art would have reason to doubt the validity and functionality of the function of the polypeptide of SEQ ID NO:2 as a vaccine or use of fragments thereof and 5) applicants have not displayed a nexus between the structure of the amino acid sequence SEQ.ID.NO: 2 and function of the polypeptide as a vaccine.

As to points 1)- 5), the specification fails to provide a written description of any immunogenic polypeptide comprising a fragment sequence of at least 15 or 20 amino acids that matches contiguous segment of SEQ.ID.NO: 2 or a polypeptide comprising the disclosed SEQ ID NO: 2 is able to be used as a vaccine. The specification fails to teach the critical polypeptide residues involved in the function of the polypeptide SEQ ID NO: 2, such that the skilled artisan is provided no guidance to test, screen or make fragments of the polypeptide comprising SEQ ID NO: 2 or the polypeptide comprising SEQ ID NO: 2, using conventional technology which allow for a vaccine use in the specification. The specification fails to teach to what extent one could alter SEQ ID NO: 2 and still present the sequence as a vaccine. The specification also fails to demonstrate the actual biological function of the polypeptide and only assigns it as a polypeptide. Even if one were to use the in vivo vaccine methodology of the specification to screen for a vaccine, one of skill in the art would be reduced to merely randomly altering amino acid(s), which would lead to unpredictable results regarding the functional activity of the polypeptide to be used as a vaccine. Moreover, polypeptide chemistry is probably one of the most unpredictable areas of biotechnology and the art teaches that the significance of any particular amino acid and sequences for different aspects of biological activity can not be predicted a priori and must be determined empirically on a case by case basis (Rudinger et al, in "PEPTIDE HORMONES", edited by Parsons, J.A., University Park Press, June 1976, page 6). The art specifically teaches that even a single amino acid change in a polypeptide leads to unpredictable changes in the biological activity of the polypeptide. For example, replacement of a single lysine residue at position 118 of the acidic fibroblast growth factor by glutamic acid led to a substantial loss of heparin binding, receptor binding, and biological-activity of the polypeptide (Burgess et al., The Journal of Cell Biology, 111:2129-2138, 1990). In transforming growth factor alpha, replacement of aspartic acid at position 47 with alanine, or asparagine did not affect biological activity while replacement with serine or glutamic acid sharply reduced the biologic activity of the mitogen (Lazar et al., Molecular and Cellular Biology, 8(3): 1247-1252, 1988). These references

demonstrate that even a single amino acid substitution or what appears to be an inconsequential chemical modification, will often dramatically affect the biological activity of a polypeptide. Polypeptides with replacement of a single amino acid residue may lead to both structural and functional changes in biological activity and immunological recognition. For example, Jobling et al. (Mol. Microbiol. 1991, 5(7): 1755-67 teaches a panel of single amino acid substitutions by oligonucleotide directed mutagenesis which products polypeptides that differ in native conformation, immunological recognition, binding and toxicity, thus exemplifying the importance of structural components to both biological function and immunological recognition. Applicants have not taught which residues of SEQ ID NO: 2 can be varied and still achieve a polypeptide that is functional as a vaccine. The specification has not conceived any other functionally equivalent polypeptide fragment and does not set forth the general tolerance to substitutions and where substitutions could be made. Since, the specification lacks a written description of any immunogenic polypeptide comprising a fragment sequence of at least 15 or 20 amino acids that matches contiguous segment of SEQ.ID.NO: 2 it is not enabled for this language because it fails to enable the skilled artisan to envision the detailed chemical structure of the claimed polypeptide fragments of SEQ ID NO: 2 as well as how to use the polypeptide fragments, one of skill in the art would be unable to produce these polypeptide fragments encompassed by the instant claims. Further, if one nucleotide is deleted or inserted at a single place within the coding sequence, all the codons down stream of that insertion or deletion will be frame shifted. The lack of enabling description of make and use a polypeptide comprising a fragment sequence of at least 15 or 20 amino acids that matches contiguous segment of SEQ.ID.NO: 2, the unpredictability associated with making and using the fragments of SEQ ID NO: 2 encompassed in the scope of the claims as set forth above, the lack of teaching even a beginning point for variation of the polypeptide sequence of SEQ ID NO: 2 for routine experimentation, lack of working examples commensurate in scope with the instant claims, the skilled artisan would be forced into undue experimentation to practice (i.e. make and use) the invention as is broadly claimed.

Claims 43-44 are drawn to a vaccine compositions. The specification provides no information on the immunogenicity of polypeptide SEQ.ID.NO: 2, the claimed fragments or the ability of such to protect from disease. The specification fails to teach that the claimed polypeptide, SEQ.ID.NO: 2 or fragments are capable of generating a humoral or cellular immune response. The specification also fails to teach that the immune/antibody response to the polypeptide produced by the polypeptide comprising an

amino acid sequence as set forth in SEQ.ID.NO: 2, alone or in combination with adjuvant or carriers provides for a protection against infection in any acceptable animal model. Vaccines by definition trigger an immunoprotective response in the host vaccinated and mere antigenic response is insufficient to provide for enablement of vaccines. This specification fails to teach any immune response generated by means of a nucleic acid --vaccine. It is well recognized in the vaccine art, that it is unclear whether an antigen(s) derived from a pathogen will elicit protective immunity. Ellis, R.W. (Chapter 29 of "VACCINES" [Plotkin, 5.A. et al. (eds) published by W. B. Saunders company (Philadelphia) in 1988, especially page 571, 2nd full paragraph] exemplifies this problem in the recitation that "The key to the problem (of vaccine development) is the identification of that polypeptide component of a virus or microbial pathogen that itself can elicit the production of protective antibodies.... and thus protect the host against attack by the pathogen". The specification fails to teach even one of the claimed polypeptide or fragments thereof alone or in combination with other antigens does in fact confer protection from infection, as is requisite of a vaccine composition. The art teaches that the selection of protective antigens from the plethora of polypeptide antigens available is unpredictable. While the specification teaches the polypeptide, the art does not recognize the claimed polypeptide or fragments thereof as therapeutic vaccines capable of conferring protection against N.meningitidis challenge in an immunized host.

The specification fails to teach that the claimed polypeptide or fragment is able to perform as a vaccine (i.e. protection, reduction in morbidity and/or mortality of disease) and the art does not recognize other similar polypeptides as operative vaccines. The courts have held that it is the specification, not the knowledge of one skilled in the art that must supply the novel aspects of an invention in order to constitute adequate enablement. (Genentech Inc. v. Novo Nordisk A/5 Ltd., 42 USPQ2d 1001). Moreover, the specification must have been enabling at the time the invention was made-and developments after the time of filing are of no consequence to what one skilled in the art would have believed at the time of filing (In re Wright, 27 U5PQ2d 1510).

The specification discloses (pages 55-56) that the polypeptide of the instant claims are intended for use as "vaccine" composition" "useful for preventing meningococcal infections." The specification, however, provides no working examples demonstrating (i.e., guidance) enablement for any *in vivo* uses of the claimed polypeptide. The induction of protective immune response (i.e., bactericidal and protective antibody response) to a meningococcal polypeptide or polysaccharide is complex and unpredictable against all meningococcal serogroups, serotypes and

> serosubtypes (see abstract of Biotecnologia Aplicada 1996, Vol 13, 1-7. The target antigen, an isolated polypeptide SEQ.ID.NO: 2 has not been shown to elicit an antibody response. Furthermore, it is unclear whether the claimed polypeptide elicits effective (i.e., protective) antibodies that are bactericidal (in vitro) and protective (in vivo) against any serogroup. Thus, an isolated polypeptide, SEQ.ID.NO: 2 as a vaccine composition in the treatment or prevention of meningococcal infections must be considered highly unpredictable, requiring a specific demonstration of efficacy of the polypeptide in any animal model.
>
> In the absence of a teaching of the claimed polypeptide can generate an immune response and that immune response is effective in prevention of disease, the specification is not be enabled for vaccines. In view of the unpredictability of the art, the lack of teachings of the specification, it would require undue experimentation on the part of the skilled artisan to practice the invention as claimed.

With respect to the pending claims, Applicants traverse this rejection. Whether the scope of enablement is sufficient is often decided in light of the following factors: (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims. In re Wands, 858 F.2d 731, 737, 8 USPQ2d 1400, 1404 (Fed. Cir. 1988). These factors are illustrative, not mandatory. Amgen, Inc. v. Chugai Pharm. Co., Ltd., 927 F.2d 1200, 1213, 18 USPQ2d 1016, 1027 (Fed. Cir. 1991). A review of these factors as applied to the present claims, supports Applicant's assertion that the claims are enabled, as outlined in subsections (A) through (G) below.

(A) *Quantity Of Experimentation*

In Reece (Reece et al., 151 J. IMMUNOL. 6175 (1993), attached as Exhibit A)[1], in excess of one thousand (1,304) overlapping 12 residue peptide fragments were synthesized by the multipin method to map T-cell epitopes of tetanus toxin. Pools of 20 peptides each were used to simplify the mapping assays. Thus, it was practical to synthesize a large number of

[1] The literature cited in this response provides evidence of the state of the art – and is not submitted under 37 CFR §1.56.

peptides, and the initial screen needed only to assay sixty to seventy pools. Pools that generated strong responses were deconvoluted by assaying the members of the pool. That such experimentation using a multipin method to screen for antigens is ordinary in this art is illustrated in CURRENT PROTOCOLS IN IMMUNOLOGY 9.7.1 (1997) (attached as Exhibit B) and Reece et al., 172 J. IMMUNOL. 241 (1994) (attached as Exhibit C). That such sequence-scanning techniques are ordinary in the art with respect to antibody-mediated antigenicity (as opposed to cellular immunity as in Reece) is illustrated in Geysen et al., 81 PROC. NATL. ACAD. SCI. USA 3998 (1984) (attached as Exhibit D).

Note that in Geysen, antisera to the whole antigen polypeptide was tested for specificity with an extensive scan of specific peptide sequences. This approach is quite useful to the present invention, where the full-length recombinant polypeptide that Applicant has synthesized can readily be used within the state of the art to produce polyclonal antibodies. These polyclonal antibodies can then be used to screen for promising smaller polypeptide antigens.

(B) *Amount Of Direction Or Guidance Presented*

Guidance in the specification can be found, for example, at page 6, lines 5-14. That the sequence-based inferences described here are ordinary in the art, and of known value in selecting positive candidates is illustrated by CURRENT PROTOCOLS IN IMMUNOLOGY 9.3.1 (1991) (attached as Exhibit E).

(C) *Presence Or Absence Of Working Examples*

An example of the recombinant expression of the full length BASB053 polypeptide is provided in the drawings as well as the working examples on pages 52-54 of the specification.

(D) *Nature Of The Invention; Predictability Or Unpredictability Of The Art*

The art is no more unpredictable than the chemical arts in general. Thus, the reasonable scope of the claims should be comparable to that which can be achieved with other structure-focused claims in the chemical arts. Moreover, the ease with which the polypeptides are screened, and the availability of robotic automation tools at the time the application was filed, counterbalance this element of the analysis.

That an unpredictable art nonetheless allows for reasonable inferences of claim scope is illustrated by the following text from the case law:

> Appellants have apparently not disclosed *every* catalyst which will work; they have apparently not disclosed *every* catalyst which will not work. The question, then, is whether in an unpredictable art, section 112 requires disclosure of a test with *every* species covered by a claim. To require such a complete disclosure would apparently necessitate a patent application or applications with "thousands" of examples or the disclosure of "thousands" of catalysts along with information as to whether each exhibits catalytic behavior resulting in the production of hydroperoxides. More importantly, such a requirement would force an inventor seeking adequate patent protection to carry out a prohibitive number of actual experiments. This would tend to discourage inventors from filing patent applications in an unpredictable area since the patent claims would have to be limited to those embodiments which are expressly disclosed. A potential infringer could readily avoid "literal" infringement of such claims by merely finding another analogous catalyst complex which could be used in "forming hydroperoxides."

Application of Angstad, 537 F.2d 498, 502-3, 190 USPQ 214, 218 (CCPA1976)(emphasis in the original).

(E) *State Of The Prior Art*

The highly advanced state of this art is illustrated by the above cited 1984 article by Geysen. The other articles discussed above clearly show that sequence scanning for antigenicity is a highly developed art.

(F) *Relative Skill Of Those In The Art*

In Enzo Biochem, Inc. v. Calgene, Inc., 188 F.3d 1362, 52 USPQ2d 1129 (Fed. Cir. 1999), the Federal Circuit approved a trial court determination in a comparable art that a person of ordinary skill would be a junior faculty member with one or two years of relevant experience or a postdoctoral student with several years of experience. Applicants respectfully submit that this level of skill is an appropriate measure of skill in the present context.

(G) *Breadth Of The Claims*

As discussed, the claims focus on a limited universe of claimed core elements. The world of these claims is miniscule compared to the monoclonal antibody world approved for claiming in In re Wands, 858 F.2d 731, 8 USPQ2d 1400 (Fed. Cir. 1988).

The Wands factors thus weigh in favor of the allowability of the present claims. Clearly the rejection of this aspect of the rejection under 35 U.S.C. §112 must be withdrawn. This indicates that the rejection under 35 U.S.C. §112 must be withdrawn with respect to claims 25-46.

To the extent the rejection asserts that some species within the scope of the claim may be inoperative, the following quote from the Board of Appeals is instructive:

> To the extent the position taken by the examiner is that the appellants' claims may include inoperative embodiments we observe that it has been held that, even assuming it could be established that the claims do embrace some inoperative embodiments, it is not the function of the claims to specifically exclude all possible inoperative substances or ineffective amounts or proportions.

While the decision giving rise to this language is not binding on future Board decisions, the decision (Ex Parte Kosley, 2002 WL 130549 (Bd.Pat.App. & Interf.) nonetheless states a correct proposition of law.

Claim Rejections under 35 U.S.C. §112, second paragraph

Claim 25 was rejected as being vague in recitation of the term, "matching." Claim 25 has been amended to more distinctly claim the present invention. In particular, claim 25 recites the terms, "comprising the sequence set forth in" and "corresponds to" and does not recite the term, "matching." Withdrawal of rejection is respectfully requested.

Claim 44 was rejected as unclear in recitation of the term, "one other N. meningitidis antigen." Claim 44 has been amended to more distinctly recite the present invention, which terms obviate this rejection. Claim 44 as amended recites that the immunogenic composition comprises at least one other *N. meninigitidis* antigen in addition to an antigen provided by the polypeptide. Withdrawal of rejection is respectfully requested.

Claim Rejections under 35 U.S.C. §102(b)

Claims 25, 27, 29, 31, 32, 43, 44 and 46 were rejected under 35 U.S.C. §102(b) as being anticipated by Martin et al. (1997 J. Ex. Med. Volume 185, No.7, April 7, 1997). In particular, the Examiner alleged:

> Martin et al disclose an isolated polypeptide, outer membrane polypeptide from whole cell lysate of OM preparations from various clinical isolates including nine meningococcal strains two of serogroup A (604A and Z4063), one of serogroup B (608B [B: 2a:P1 .2: L3]), two of serogroup C (2241C and 59C), one of serogroup 29-E, one of serogroup W-135, one of serogroup Y (SLATY) and one of serogroup Z (SLATZ) (page 1174, under materials and method, antigens). Monoclonal antibodies were produced by immunizing mice with OM preparation indicating that the disclosed isolated polypeptides are immunogenic and thus read on claim 46. Applicant's use of the open-ended term "comprising" in the claims fails to exclude unrecited steps or ingredients and leaves the claims open for inclusion of unspecified ingredients, even in major amounts. Whole cell lysates prepared in buffer (pharmaceutical carrier) from N.meningitidis inherently comprise the amino acid sequence as set forth in the SEQ.lD.NO: 2 and several N.meningitidis antigens. *See In re Horvitz, 168 F 2d 522, 78 U.S.P.Q. 79 (C.C.P.A. 1948)* and Ex parte Davis et al., 80 U.S.P.Q. 448 (PTO d. App. 1948). In the absence of evidence to the contrary the claimed isolated polypeptide comprising SEQ.lD.NO: 2 is inherent in the preparations of the disclosed prior art polypeptide. Since the Office does not have the facilities for examining and comparing applicants' claimed isolated polypeptide comprising SEQ.ID.NO: 2, with the polypeptide of prior art, the burden is on applicant to show a novel or unobvious difference between the claimed product and the product of the prior art. *See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.*
>
> It is acknowledged that weight is given to every term in claims 43-44. This is why the instant claims drawn to immunogenic composition i.e., vaccine is scrutinized differently from a composition claim under 112, first paragraph. However, under prior art rejections, the term vaccine must be weighed with the structural limitations of the claim. Therefore, the examiner is considering vaccine composition as an isolated polypeptide comprising SEQ.ID.NO: 2. If the immunogenic composition i.e., vaccine merely comprises a known composition (i.e., an isolated polypeptide), the term carries little weight absent evidence of structural difference. Of course, the existence of an unobvious structural difference would define over the prior art. Therefore,

> Martin et al meet the immunogenic/vaccine composition limitation of the claims 43-44. See In re Best, 562 F.2d 1252, 195 USPQ 430 (CCPA 1977) and In re Fitzgerald et al., 205 USPQ 594.

Applicant respectfully disagrees. A claim is anticipated only if each and every element is found, either expressly or inherently described, in the reference. *See* MPEP 2131. Moreover, the identical invention must be shown in as complete detail as is contained in the claim. Applicant submits that Martin et al. does not identically disclose SEQ ID NO:2 of the present invention, fusion proteins of SEQ ID NO:2, or fragments of SEQ ID NO:2. In fact, Martin et al. does not disclose any amino acid sequences at all. Martin et al merely discloses an outer membrane protein from whole cell lysate. Abiding by these standards, Martin et al. does not anticipate the invention as presently claimed. Accordingly, reconsideration of the rejection is respectfully requested.

FEE DEFICIENCY

☒ If an extension of time is deemed required for consideration of this paper, please consider this paper to comprise a petition for such an extension of time. The Commissioner is hereby authorized to charge the fee for any such extension to Deposit Account No. 50-0258.

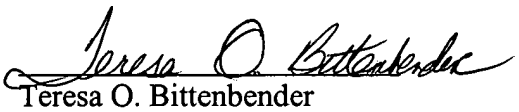
and/or

☒ If any additional fee is required for consideration of this paper, please charge Account No. 50-0258

Closing Remarks

Applicants thank the Examiner for the Office Action and believe this response to be a full and complete response to such Office Action. Accordingly, favorable reconsideration in view of this response and allowance of the pending claims are earnestly solicited.

Respectfully submitted,



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Appendix A

Claims following entry of amendment mailed June 10, 2003

25. (amended) An isolated polypeptide comprising a member selected from the group consisting of

(a) an amino acid sequence comprising the sequence set forth in ~~matching~~ SEQ ID NOs:2 or 4;

(b) an immunogenic polypeptide comprising a fragment sequence of at least 15 amino acids that corresponds to ~~matches~~ an aligned contiguous segment of SEQ ID NOs:2 or 4,

wherein the isolated polypeptide, when administered to a subject in a suitable composition which can include an adjuvant, or a suitable carrier coupled to the polypeptide, induces an antibody or T-cell immune response to a polypeptide having the sequence of SEQ ID NOs:2 or 4.

26. (withdrawn)

27. (original) The isolated polypeptide of claim 25, wherein the polypeptide is according to (a).

28. (withdrawn)

29. (original) The isolated polypeptide of claim 25, wherein the polypeptide is according to (b).

30. (withdrawn)

31. (original) The isolated polypeptide of claim 25, wherein the immunogenic fragment of (b) comprises at least 20 amino acids.

32. (original) The isolated polypeptide of claim 25, wherein the amino acid sequence of (a) is according to SEQ ID NO:2.

33. (withdrawn)

34. (withdrawn)

35. (withdrawn)

36. (withdrawn)

37. (withdrawn)

38. (withdrawn)

39. (withdrawn)

40. (withdrawn)

41. (withdrawn)

42. (withdrawn)

43. (currently amended) An immunogenic composition ~~A vaccine~~ comprising the polypeptide of Claim 25 and a pharmaceutically acceptable carrier.

44. (currently amended) The immunogenic composition ~~vaccine~~ of Claim 41, wherein the immunogenic composition ~~vaccine~~ comprises at least one other *Neisseria meningitidis* antigen in addition to an antigen provided by the polypeptide.

46. (original) A method for inducing an immune response in a mammal comprising administration of the polypeptide of Claim 25.

Appendix B:

Abstract

The invention provides BASB053 polypeptides and polynucleotides encoding BASB053 polypeptides and methods for producing such polypeptides by recombinant techniques. Also provided are diagnostic, prophylactic and therapeutic uses.

B2

Appendix C

I claim:

Appendix D

BRIEF DESCRIPTION OF THE DRAWINGS

FIG. 1 is an alignment of the BASB053 polynucleotide sequences; identity to SEQ ID NO:1 is indicated by a dot; gaps are indicated by a dash.

FIG. 2 is an alignment of the BASB053 polypeptide sequences; identity to SEQ ID NO:2 is indicated by a dot; gaps are indicated by a dash.

FIG. 3 is an SDS-PAGE electrophoresis showing expression of recombinant BASB053 in E. coli Top10 cells; lane 1 corresponds to bacterial protein extracts (strain carrying plasmid pBADgIII); lane 2 corresponds to recombinant protein (pBADgIII-BASB053).